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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,690	01/18/2002	Scot R. Sheppard	2001.690 US/C1	3779
31846	7590	02/11/2004		
			EXAMINER	
			MOHAMED, ABDEL A	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,690	SHEPPARD, SCOT R.	
	Examiner Abdel A. Mohamed	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 15 July 2002.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-15 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

**ACKNOWLEDGMENT OF PRIORITY, PRELIMINARY AMENDMENT, IDS, STATUS
OF THE APPLICATION AND CLAIMS**

1. This application is Continuation-in-part (CIP) of Application No. 09/766,043 having a filing date of 1/19/01, now abandoned. The Information Disclosure Statements (IDS) and Form PTO-1449 filed 7/15/02 and the preliminary amendment filed 6/18/02, respectively are acknowledged, entered and considered. In view of Applicant's request claims 5-7 and 11-12 (See Rule 126 below) have been amended and claims 14 and 15 (See Rule 126 below) have been added. Thus, claims 1-15 are now pending in the application.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. In the instant case, after claim 10, the next claim following claim 10 is claim 12 (i.e., there is no claim 11). Thus, misnumbered claims 12-14 have been renumbered 11-13. When new claims are presented, they must be renumbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). The highest numbered claim previously presented after correction in accordance with 37 CFR 1.126 is claim 13. Hence newly presented claims 15-16 have been renumbered as claims 14 and 15.

OBJECTIONS TO TRADEMARKS AND THEIR USE

2. The use of trademark "Y-PER®" has been noted in this application. Although, the use of trademark is permissible in patent applications, the proprietary nature of the mark should be respected and every effort made to prevent its use in a manner, which might adversely affect their validity as trademark.

Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description is inherent in the article referred by the trademark. This description requirement is made because the nature and composition of articles denoted by trademark can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. § 112 ^{2nd} PARGRAPH

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear as to whether "the active ingredient is charged amine acids" is in the detergent or in the reducing agent or is separate from each of the detergent and the reducing agent. Appropriate clarification is required.

1. Claim 1 recites the limitation "the active ingredient" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "the suspended host cells" in lines 1-2. There is insufficient antecedent basis for this limitation in claim 1 or claim 4.

Claim 5 is indefinite in the recitation "0.01" because it is not clear to what unit the number refers. If it is to percentage, then, amendment of the claim to recite "0.01 percent" is suggested.

Claim 5 is indefinite and vague in the recitation " the solubility limit of the detergent" because it is not clear to which detergent the claim is referring. Further, the solubility limit of the detergent is not disclosed or described neither in the specification nor in the claim. Appropriate clarification is required.

Claims 11, 13, 14 and 15 recite the limitation "the solution" in line 1 of claims 11, 13 and 15 and in line 2 of claim 14, respectively. There is insufficient antecedent basis for this limitation in claim 1 or claim 11 or claim 13 or claim 14 or claim 15.

CLAIMS REJECTION-35 U.S.C. § 102(b)

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Horowitz et al. (Blood, Vol. 79, No. 3, pp. 826-831, 1992).

Horowitz et al. discloses a method of releasing a protein of interest from host cells comprising contacting or lysing the cells with a reducing agent and a detergent, wherein the detergent is an amphipathic charged amine or amineoxide such as tributylphosphate (TNBP) and the detergent is not dimethyltrideacylamine (See pages 826 and 830) as directed to claims 1-3. On page 827, the reference discloses the incubation of the cell and detergent and reducing agent mixtures at least for 4 hours at a temperature of 30⁰ C, and as such overlaps with the limitations of claims 11-13. Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 1-3 and 11-13 as drafted.

5. Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Horowitz et al. (Transfusion, Vol. 25, No. 6, pp. 516-522, 1985).

Horowitz et al. discloses a method of releasing a protein of interest from host cells comprising contacting or lysing the cells with a reducing agent and a detergent, wherein the detergent is an amphipathic charged amine or amineoxide such as tributylphosphate (TNBP) and the detergent is not dimethyltrideacylamine (See pages 516-517) as directed to claims 1-3. On page 57 and Table I, the reference discloses the incubation of the cell and detergent and reducing agent mixtures for 3-18 4 hours at a temperature of 4⁰ C to ambient temperature of 22-24⁰ C, and as such overlaps with the limitations of claims 11-13. Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 1-3 and 11-13 as drafted.

6. Claims 1-3, 11-13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Piet et al. (Transfusion, Vol. 30, No. 7, pp. 591-598, 1990).

Horowitz et al. discloses a method of releasing a protein of interest from host cells comprising contacting or lysing the cells with a reducing agent and a detergent, wherein the detergent is an amphipathic charged amine or amineoxide such as tributylphosphate (TNBP) and the detergent is not dimethyltrideacylamine (See page 591) as directed to claims 1-3. On pages 592-593 and Table II, the reference discloses the incubation of the cell and detergent and reducing agent mixtures for at least 4 hours at a temperature of 30⁰ C, and as such overlaps with the limitations of claims 11-13. With respect to the pH solution of claim 15, on page 592, right column, the reference discloses the use of pH ranges of 6.5 to 7.4, and as such meets the limitation of claim 15. Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 1-3, 11-13 and 15 as drafted.

CLAIM REJECTIONS-35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable Yamazaki (U.S. Patent No. 5,011,915) taken with Builder et al. (U.S. Patent No. 5,407,810).

The primary reference of Yamazaki teaches a method of releasing and/or purifying a protein of interest from recombinant pre S1/S2 hepatitis B antigen or portion thereof, comprising the steps of contacting the host cells such as *Pichia pastoris* cells with a reducing agent (e.g., cysteine, DTT, DTE, etc.) and a detergent (e.g., TRITON X-100 and TPCK). The purification steps for the purpose of reducing proteolysis is carried out at about 4⁰ C (See e.g., cols. 4-9) as directed to claims 1-3, 8, 10 and 13. The primary reference discloses on col. 7, lines 32-55, the ranges of the concentrations of the detergents to be between 0.01 2 % (w/v) and the preferable concentration is about 0.5 % (w/v) which overlaps the claimed ranges of claims 5-7. With respect to the limitation of the concentration of the detergent of claim 14, the primary reference on col. 7, lines 50-55 clearly states that given the teachings of the reference, it is within the ordinary skill of the art to adapt or adjust the desired exact concentration in a formulation of interest. Thus, in view of this, the selection of the appropriate concentration of a solution would have been optimization of the art recognizable variation. Therefore, the primary reference similarly teaches a process of releasing a protein, recombinant or otherwise from a cell by contacting a host cell containing a protein of interest with a solution comprising one or more detergents and one or more reducing agents.

The reference of Yamazaki differs from claims 1-15 in not teaching the use of organic solvents such as glycerol for suspension of host cells and the specific concentrations of detergents, glycerols and reducing agents. Although, the primary reference does not teach the use of glycerol as detergent, but the reference clearly suggests the use of other organic solvents by stating that suitable agents include detergents or protein denaturants, or mixtures thereof. A variety of neutral or nonionic detergents can be used, including but not limited to detergents of nooxynol series, octoxynol series, polyoxyethylene series, etc. (See e.g., col. 6, lines 59-66). However, the secondary reference of Builder et al. teaches the use of organic solvents such as glycerol (See e.g., Col. 17, lines 17-23) as directed to claim 4, and reducing agents such as DDT and cysteine for the intended purpose of lysing cells to obtain a protein of interest from recombinant products or others, wherein the incubation is carried out at 20-40⁰ C for about 1-12 hours (See e.g., col. 20) as directed to claims 4, 8 and 11-13. The preferred concentration of the reducing agent is about 1-5 mM, the preferred concentration of glycerol is about 1-4 M (See col. 20, lines 24-32) as directed to claim 9. Thus, the secondary reference shows the exemplary and the preferred ranges for the detergent and reducing agents, which overlap, with the claimed ranges. Hence, the ranges disclosed in the prior art and claimed by Applicant overlap in scope, and as such it is conventional and within the ordinary skill in the art to optimize or select specific detergent or reducing agent concentrations from the ranges disclosed.

Thus, one of ordinary skill in the art would have been motivated at the time the invention was made to apply the teachings of the secondary reference of Builder et al.

(i.e., use of organic solvent detergent such as glycerol with specific concentrations of reducing agents and detergents) to the primary reference of Yamazaki because such features are known or suggested in the art, as seen in the secondary reference, and including such features of using organic solvents such as glycerol into the method of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

Therefore, the combined teachings of the prior art makes obvious the claimed invention's process of recovering intracellular protein of interest fro a cell by contacting the cell with a solution comprising one or more detergents and one or more reducing agents, absent of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The appropriate fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

Christopher S. F. Low
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AAM Mohamed/AAM

February 9, 2004